REMARKS

Claims 1-5, 9, 15 and 35-47 are now pending. Claims 6-8, 10-14 and 16-34 have been cancelled without prejudice or disclaimer. A "clean" claim set is provided above. Amendments to the claims are indicated in the section entitled "Version Showing Changes Made", which follows the remarks.

Claim 1 has been amended to recite that the cell expresses one or more of a specified group of expression profile genes. Support is found, for example, at page 2, lines 10-17, page 13 , lines 1-2 and figure 72, page 9, lines 13-14 and figure 32, of the specification as filed.

Claim 9 has been amended to state that step a) entails determining a gene selected from a specified group. Support is found as described in the amendment to Claim 1. Claim 9 has also been amended to specify that the expression in the second individual may be in normal or breast cancer tissue and the comparison is indicative. Support is found, for example, at page 40, line 27 to page 41, line 7.

Claim 38 has been added as a claim depending from Claim 9, specifying the second tissue type of the first individual. Support is found, for example, at page 40, line 27 to page 41, line 7.

Claim 39 has been added as a claim depending from Claim 38, specifying the indication. Support is found, for example, at page 41, lines 3-7.

Claim 40 has been added as a claim depending from Claim 9, specifying the second tissue type of the first individual. Support is found, for example, at page 9, lines 20-21 and figure 36.

Claim 41 has been added as a claim depending from Claim 40, specifying the indication. Support is found, for example, at page 41, lines 3-7.

Claim 42 has been added as a claim depending from Claim 9, specifying the tissue type of the second individual. Support is found, for example, at page 41, lines 3-7.

Claim 43 has been added as a claim depending from Claim 42, specifying the indication. Support is found, for example, at page 41, lines 3-7.

Claim 44 has been added as a claim depending from Claim 9, specifying the tissue type of the second individual. Support is found, for example, at page 40, line 27 to page 41, line 7.

Claim 45 has been added as a claim depending from Claim 44, specifying the indication. Support is found, for example, at page 41, lines 3-7.

Claim 46 has been added as a claim depending from Claim 9, specifying the mode of determining expression. Support is found, for example, at page 42, lines 6-8.

Claim 47 has been added as a claim depending from Claim 46, specifying the mode of measuring. Support is found, for example, at page 42, lines 9-13.

Restriction Requirement

Claims 1-37 are subject to a restriction requirement. The Examiner has determined that the claims represent 19 distinct inventions designated in the following groups of claims:

I. Claims 1-3, directed to a method of screening drug candidates.

II. Claim 4, directed to a method of screening for a bioactive agent capable of binding a breast cancer modulating protein (BCMP).

III. Claim 5, directed to a method of screening for a bioactive agent capable of modulating a BCMP.

IV. Claims 6-7, directed to a method of evaluating the effect of a breast cancer drug.

V. Claim 8, directed to a biochip.

VI. Claim 9, directed to a method of diagnosing breast cancer.

VII. Claims 10-14, directed to an antibody.

VIII. Claim 15, directed to a method of screening for agents that inhibit binding of an antibody to a BCMP.

IX. Claims 16-21, directed to a method of inhibiting breast cancer.

X. Claim 22, directed to a method of inhibiting breast cancer.

XI. Claims 23-24, directed to a peptide and composition comprising same.

XII. Claims 25-26, directed to a peptide and composition comprising same.

XIII. Claim 27, directed to a method of eliciting an immune response.

XIV. Claim 28, directed to a method of eliciting an immune response.

XV. Claim 29, directed to a composition capable of eliciting an immune response.

XVI. Claim 30, directed to a composition capable of eliciting an immune response.

XVII. Claim 31-34, directed to a method of treating breast cancer.

XVIII. Claims 35-36, directed to a method of determining the prognosis of an individual with breast cancer.

XIX. Claim 37, directed to methods of neutralizing the effect of a BCMP.

Applicants hereby elect Group VI, namely Claim 9, for further prosecution, with traverse. In traversal, applicants submit that the present restriction requirement has not shown that a serious burden exists for examining all of the pending claims.

Applicants first point out that the language of 35 U.S.C. § 121 states that restriction may be required if two or more independent and distinct inventions are claimed. Applicants emphasize the requirement of both independence and distinctness, not one or the other in the alternative. The statute is the controlling law and the plain meaning of the statute is clear, notwithstanding the analysis presented in MPEP § 802.01. Applicants also note that, according to MPEP § 803, "If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions." While the language of the statute is permissive, the language in the MPEP is not, but rather demands that the entire application be examined if it can be done without serious burden. Therefore, even if claims are found to be separate and distinct, this is not sufficient to demand restriction. A showing of serious burden must also be made.

MPEP § 803 goes on to say that a *prima facie* showing of serious burden is found "if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search". MPEP § 808.02 is cited as defining what is meant by these three categories of separation/differentiation. Classification, it is assumed, refers to the

U.S. Patent Classification System. However, MPEP § 803 refers only to a difference in classification, not subclassification. Therefore, inventions in the same class must find a showing in the other two categories. Separate status in the art requires a showing that a separate subject for inventive effort has been established, the MPEP stating that citation of patents may be used to show separate status. Showing of a different field of search requires that it is necessary to search in places pertinent to one separate and distinct invention where no pertinent art to the other exists.

Applicants have elected Group VI for further prosecution, which is classified in class 435. Groups I-III, VIII, XVIII and XIX also in class 435. Therefore, a showing in one of the other two categories (different status or separate field of search) must be made by the Examiner for the restriction requirement of the cited claims to be proper.

The Examiner asserts that Groups I-III, VI, VIII, XVII and XVIII are "patentably distinct because they have different objectives and require different process steps." However, this does not establishes that they have separate status or require a different field of search. No patents indicating separate status are cited. No showing is made that search is required in a place pertinent to one group that is not pertinent to any or all of the others.

The Office Action concludes that the designated groups "have acquired a separate status in the art as shown by there different classification and recognized divergent subject matter, and because Inventions I-XIX require different searches that are not co-extensive". Applicants submit that reliance on different classification does not distinguish Groups I-III, VI, VIII, XVII and XVIII. Furthermore, having a different method step or even a different objective does not establish a different status in the art. As Applicants pointed out above, no support, such as issued patents, are presented to establish the claims of the different designated groups as having separate status in the art. Finally, whether searches for the different designated groups are "co-extensive" or not is not relevant to the question of whether a different field of search is required. The test is whether a search must be made in a place for one group where no art pertinent to the other group would be found. No evidence is presented to establish that any search pertinent to one of Groups I-III, VI, VIII, XVII and XVIII group would not also produce some art pertinent to any or all of the others. Applicants submit that

a showing of serious burden has not been made so as to prevent inclusion of all of Groups I-III, VI, VIII, XVII and XVIII in examination on the merits, based on the restriction guidelines found in the MPEP.

Additionally, although the amendments make the issue moot, with all due respect, Applicants submit that the Office Action is improper with regard to the species election for Groups I and VIII (Claims 1-3 and 15, respectively). Claim 1 is written as a Markush group. The Examiner appears to be treating Claim 15 similarly. However, the treatment of these claims is not consistent with PTO practice, as set out in MPEP § 803.02. "If the members of the Markush group are sufficiently few in number . . . that a search and examination of the entire claim may be made without serious burden, the examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions." (MPEP § 803.02). The Markush Group of Claim 1 had only 10 members. Applicants submit that 10 species is sufficiently few to allow examination of all. Furthermore, MPEP § 803.02 describes the proper procedure in the event of a determination that a Markush group includes independent and distinct inventions. "In applications of this nature, the examiner may require a provisional election of a single species prior to examination on the merits. . . . [S]hould no prior art be found that anticipates or renders obvious the elected species, the search of the Markush group will be extended." The Examiner did not request a provisional election. And, contrary to the Examiner's statement, each member of a Markush group is a species, as each is functionally interchangeable in the claim.

Relevant to the discussion above and the amendments made, Applicants direct the Examiner's attention to 1192 OG 68 (November 19, 1996). In the Notice entitled "Examination of Patent Applications Containing Nucleotide Sequences", the policy of the PTO is clearly laid out. The Examiner is particularly directed to the title of Part II, "The PTO Will Permit Applicants to Claim Up to Ten Independent and Distinct Nucleotide Sequences In One National Application". Applicants assert that the plain meaning of this title, further supported by the text that follows it, is that the discretion is up to the Applicants to Claim up to ten sequences. To Applicants' knowledge, no change in PTO policy has been published, in the OG or anywhere else. Applicants submit that, until a change in PTO has been officially

announced and the public has had an opportunity to comment, they should be permitted to claim up to 10 nucleotide sequences in the present application. Therefore, Applicants respectfully request the Examiner to examine all sequences recited in the claims.

Applicants submit that the application is now in form for examination on the merits and subsequent allowance. If the Examiner believes that there are remaining issues that may be disposed of by telephone, she is invited to called the undersigned attorney at (415) 781-1989.

Respectfully submitted,

FLEHR, HOHBACH, TEST,
ALBRITTON & HERBERT

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James J. Diehl

James J. Diehl, Reg. No. 47,527 for:
David J. Brezner, Reg. No. 24,774

Four Embarcadero Center
Suite 3400
San Francisco, CA 94111-4187
Telephone: (415) 781-1989

VERSION SHOWING CHANGES MADE

1. (Amended) A method of screening drug candidates comprising:
a) providing a cell that expresses an expression profile gene [which encodes a protein] selected from the group consisting of [BCH1, BCA2, BCJ7, BCN1, BCN5, BCO2, BCQ5, BCR2, BCX2 and BCY3] SEQ ID NOS: 51, 23 or a fragment thereof;
b) adding a drug candidate to said cell; and
c) determining the effect of said drug candidate on the expression of said expression profile gene.

2. A method according to claim 1 wherein said determining comprises comparing the level of expression in the absence of said drug candidate to the level of expression in the presence of said drug candidate, wherein the concentration of said drug candidate can vary when present, and wherein said comparison can occur after addition or removal of the drug candidate.

3. A method according to claim 1 wherein the expression of said profile gene is decreased as a result of the introduction of the drug candidate.

4. A method of screening for a bioactive agent capable of binding to a breast cancer modulator protein (BCMP), wherein said BCMP is BCH1 or a fragment thereof, said method comprising combining said BCMP and a candidate bioactive agent, and determining the binding of said candidate agent to said BCMP.

5. A method for screening for a bioactive agent capable of modulating the activity of a breast cancer modulator protein (BCMP), wherein said BCMP is BCH1 or a fragment thereof, said method comprising combining said BCMP and a candidate bioactive agent, and determining the effect of said candidate agent on the bioactivity of said BCMP.

Claims 6-8 have been cancelled without prejudice or disclaimer.

9. (Amended) A method of diagnosing breast cancer comprising:
a) determining the expression of [a gene encoding BCH1] one or more genes selected from the group consisting of a gene comprising the nucleic acid sequence of one of SEQ ID NOS: 51, 23 or a fragment thereof in a [first tissue type] breast tissue sample of a first individual; and
b) comparing said expression [of said gene from] to expression of said gene(s) in a second normal tissue type from said first individual or a second [unaffected] tissue type of a second individual;
wherein [a difference in said expression] said comparison indicates that the first individual has breast cancer.

Claims 10-14 have bee cancelled without prejudice or disclaimer.

15. (Amended) A method for screening for a bioactive agent capable of interfering with the binding of a breast cancer modulator protein (BCMP) or a fragment thereof, wherein said BCMP is BCH1, and an antibody which binds to said BCMP or fragment thereof, said method comprising:

a) combining a BCMP or fragment thereof, a candidate bioactive agent and [and] an antibody which binds to said BCMP or fragment thereof; and

b) determining the binding of said BCMP or fragment thereof and said antibody.

Claims 16-34 have been cancelled without prejudice or disclaimer.

35. A method for determining the prognosis of an individual with breast cancer comprising determining the level of BCH1 in a sample, wherein a high level of BCH1 indicates a poor prognosis.

36. A method for determining whether an individual with breast cancer will be non-responsive to anti-estrogen therapies comprising determining the level of BCH1 wherein a high level of BCH1 indicates that an individual will be non-responsive.

37. A method of neutralizing the effect of a BCH1, or a fragment thereof, comprising contacting an agent specific for said protein with said protein in an amount sufficient to effect neutralization.

The following new claims have been added:

--38. (New) The method of Claim 9, wherein said second normal tissue type from said first individual is breast tissue.

39. (New) The method of Claim 38, wherein a difference between expression in said breast tissue sample of said first individual and said second normal tissue type indicates that the first individual has breast cancer.

40. (New) The method of claim 9, wherein said second normal tissue type of said first individual is not breast tissue.

41. (New) The method of Claim 40, wherein a difference between expression in said breast tissue sample of said first individual and said second normal tissue type indicates that the first individual has breast cancer.

42. (New) The method of Claim 9, wherein said second tissue type of said second individual is normal breast tissue.

43. (New) The method of Claim 42, wherein a difference between expression in said breast tissue sample of said first individual and said second tissue type indicates that the first individual has breast cancer.

44. (New) The method of Claim 9, wherein said second tissue type of said second individual is breast cancer tissue.

45. (New) The method of Claim 44, wherein a similarity between expression in said breast tissue sample of said first individual and said second tissue type indicates that the first individual has breast cancer.

46. (New) The method of Claim 9, wherein said determining is by measuring RNA comprising the RNA equivalent of a sequence selected from the group consisting of SEQ ID NOS: 51, 23.

47. (New) The method of Claim 46, wherein said measuring utilizes a biochip comprising one or more nucleic acids comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 51, 23 or a fragment thereof.--